

**CLAIMS:**

1. A complex that comprises a narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof, and
  - (i) a substance that has pharmacological activity against a pathogenic organism,
  - 5 or
  - (ii) a substance that has pharmacological activity against a cancer, or
  - (iii) one or more agents selected from antigens and immunogens.
2. A complex as claimed in claim 1, wherein the pathogenic organism is  
10 predominantly but not exclusively an intracellular organism.
3. A complex as claimed in claim 2, wherein the pathogenic organism is an intracellular organism that exists and/or persists in cells of macrophage origin and/or in other antigen presenting cells such as dendritic cells.  
15
4. A complex as claimed in claim 1, wherein the pathogenic organism is selected from the following organisms :
  - a) Organisms that cause superficial mycoses, including ringworm; tinea; thrush;  
20 Malassezia infections, including pityriasis versicolor, Malassezia folliculitis, seborrhoeic dermatitis and Scytalidium infections; Otomycosis; and Keratomycosis.
  - b) Candida species that cause invasive and chronic fungal infections, including  
25 Candida albicans, Candida tropicalis and Candida glabrata; Aspergillus species, including Aspergillus fumigatus, Aspergillus flavus and Aspergillus niger; Cryptococcus neoformans; Mucormycosis, for example, caused by species of Absidia, Rhizopus and Rhizomucor; Fusarium species; Trichosporon species; Blastomycosis; Sporothrix species; Sporotrichum species; Histoplasmosis, for  
30 example, caused by Histoplasma capsulatum var. capsulatum; African histoplasmosis, for example, caused by Histoplasma capsulatum var. duboisii; Blastomycosis, for example, caused by Blastomyces dermatitidis; Coccidioidomycosis, for example, caused by Coccidioides immitis;

- 84 -

Paracoccidioidomycosis, for example, caused by *Paracoccidioides brasiliensis*; and Infections caused by *Penicillium marneffei*.

5 c) Organisms that cause mycobacterial diseases, for example, tuberculosis and leprosy caused by members of the mycobacterial family, for example, *Mycobacterium tuberculosis*, atypical mycobacteria, and *Mycobacterium leprae*.

10 d) Members of the schistosoma family that cause Schistosomiasis, for example, *Schistosoma haematobium*, *Schistosoma mansoni*, *Schistosoma japonicum*, *Schistosoma intercalatum*, and *Schistosoma mekongi*.

e) Organisms that cause typhoid and paratyphoid fevers, for example, members of the salmonella family of serotypes A, B, C and D.

15 f) Organisms that cause toxoplasmosis, for example, *Toxoplasma gondii*.

g) Organisms that cause Human African Trypanosomiasis, for example, *Trypanosoma brucei gambiense* or *Trypanosoma brucei brucei*.

20 h) Organisms that cause American Trypanosomiasis, for example, *Trypanosoma cruzi*.

i) Organisms that cause malaria, for example, *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale* and *Plasmodium malariae*.

25

j) Organisms that cause HIV and HTLV infections.

k) Organisms that cause *Pneumocystis carinii* infections.

30 5. A complex as claimed in claim 1, wherein the pathogenic organism causes leishmaniasis.

- 85 -

6. A complex as claimed in claim 1, wherein the substance that has pharmacological activity against the pathogenic organism is capable of killing or disrupting an organism as defined in any one of claims 2 to 5.
- 5 7. A complex as claimed in claim 6, wherein the pharmacologically active substance is amphotericin B.
8. A complex as claimed in claim 1, wherein an antigen or immunogen is derived directly or indirectly from an organism that causes tuberculosis, tetanus,  
10 anthrax, cholera, diphtheria, measles, mumps, rubella, Hepatitis A, Hepatitis B, influenza, herpes zoster, poliomyelitis, rabies, smallpox, yellow fever, varicella, herpes zoster, herpes simplex, influenza or leishmaniasis.
9. A complex as claimed in claim 1, wherein an antigen or immunogen is  
15 derived directly or indirectly from *Haemophilus influenzae* type B, *Neisseria meningitidis*, *Bordetella pertussis*, *Streptococcus pneumoniae*, or *Salmonella typhi*.
10. A complex as claimed in claim 1, wherein an antigen or immunogen is derived directly or indirectly from an organism as defined in any one of claims 2 to  
20 6.
11. A complex as claimed in claim 1, claim 9 or claim 10, wherein an antigen or immunogen is obtained from a natural source, or has been produced by recombinant DNA technology or by chemical synthesis, or by any one or more of  
25 said methods.
12. A complex as claimed in claim 1, wherein the substance that has pharmacological activity against a cancer is a cytotoxic agent.
- 30 13. A pharmaceutical preparation which comprises a complex as claimed in any one of claims 1 to 12 in admixture or conjunction with a pharmaceutically suitable carrier.

- 86 -

14. A pharmaceutical preparation as claimed in claim 13, which comprises a delivery system adjuvant.

5 15. A complex as claimed in any one of claims 1 to 14 for use as a medicament.

10 16. A complex for use in treatment of an infection by a pathogenic organism and/or for inducing an immune response to the pathogenic organism, which complex comprises a narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof and a substance that has pharmacological activity against the pathogenic organism.

15 17. A method of treating an infection by a pathogenic organism in a subject in need of such treatment, which comprises administering to the subject a therapeutically effective amount of a complex comprising a narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof and a substance that has pharmacological activity against the pathogenic organism.

20 18. A method of inducing an immune response to the pathogenic organism in a subject in need thereof, which comprises administering to the subject an effective amount of a complex comprising a narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof and a substance that has pharmacological activity against the pathogenic organism.

25 19. A complex or a method as claimed in any one of claims 16 to 18, wherein the pathogenic organism is as defined in any one of claims 2 to 5.

30 20. A complex or a method as claimed in any one of claims 16 to 18, wherein the substance that has pharmacological activity against the pathogenic organism is as defined in claim 6.

- 87 -

21. A complex or a method as claimed in any one of claims 16 to 18, for treatment of leishmaniasis and/or for inducing an immune response to an organism that causes leishmaniasis in any of its clinical forms.
- 5 22. A complex or a method as claimed in claim 21, wherein the substance that has pharmacological activity against an organism that causes leishmaniasis is amphotericin B.
23. A complex or a method as claimed in any one of claims 16 to 22, wherein  
10 the immune response comprises therapeutic and/or prophylactic vaccination against the pathogenic organism.
24. A complex for use in treatment of a cancer, which complex comprises a narrow molecular weight distribution polymer that includes units derived from an  
15 acrylic acid or a salt thereof and a substance that has pharmacological activity against the cancer.
25. A method of treating a cancer in a subject in need of such treatment, which comprises administering to the subject a therapeutically effective amount of a  
20 complex comprising a narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof and a substance that has pharmacological activity against the cancer.
26. A method of inducing an immune response to a cancer in a subject in need  
25 thereof, which comprises administering to the subject an effective amount of a complex comprising a narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof and a substance that has pharmacological activity against the cancer.
- 30 27. A complex or a method as claimed in any one of claims 24 to 26, wherein the substance that has pharmacological activity against the cancer is a cytotoxic agent.

- 88 -

28. A complex or a method as claimed in any one of claims 24 to 27, wherein the immune response comprises therapeutic and/or prophylactic vaccination against the cancer.
- 5 29. A complex that comprises a polymer including units derived from an acrylic acid or a salt thereof and one or more agents selected from antigens and immunogens, for inducing an immune response to the antigen or immunogen.
- 10 30. A method of inducing an immune response to an antigen or immunogen in a subject, which comprises administering to the subject an effective amount of a complex comprising a narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof and the antigens or immunogen.
- 15 31. A complex or a method as claimed in any one of claims 10 to 12, wherein the antigen or immunogen is derived directly or indirectly from an organism against which a protective immune response is required.
- 20 32. A complex or a method as claimed in claim 29 or claim 30, wherein the antigen or immunogen is as defined in any one of claims 8 to 11.
- 25 33. A complex or a method as claimed in any one of claims 29 to 32, wherein the immune response comprises therapeutic and/or prophylactic vaccination against the pathogenic organism.
- 30 34. A narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof for use with a substance that has pharmacological activity against a pathogenic organism for the treatment of an infection by the pathogenic organism and/or for inducing an immune response to the pathogenic organism.
35. A method of treating an infection by a pathogenic organism in a subject in need of such treatment, which comprises administering to the subject therapeutically effective amounts of a narrow molecular weight distribution

- 89 -

polymer that includes units derived from an acrylic acid or a salt thereof and a substance that has pharmacological activity against the pathogenic organism.

36. A method of inducing an immune response to the pathogenic organism in a  
5 subject in need thereof, which comprises administering to the subject effective amounts of a narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof and a substance that has pharmacological activity against the pathogenic organism.

10 37. A polymer as claimed in claim 34 or a method as claimed in claim 36, wherein the immune response comprises therapeutic and/or prophylactic vaccination against the pathogenic organism.

15 38.. A polymer or a method as claimed in any one of claims 34 to 37, wherein the pathogenic organism is as defined in any one of claims 2 to 5.

39. A polymer or a method as claimed in any one of claims 34 to 38, wherein the substance that has pharmacological activity against the pathogenic organism is as defined in claim 6.

20

40. A polymer or a method as claimed in any one of claims 34 to 37 for treatment of leishmaniasis and/or for inducing an immune response to an organism that causes leishmaniasis in any of its clinical forms.

25 41. A polymer or a method as claimed in claim 40, wherein the substance that has pharmacological activity against the organism that causes leishmaniasis is amphotericin B.

30 42. A narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof for use with one or more agents selected from antigens and immunogens for inducing an immune response to the antigen or immunogen.



- 90 -

43. A method of inducing an immune response to an antigen or immunogen in a subject in need of such treatment, which comprises administering to the subject therapeutically effective amounts of a narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof and the antigen or immunogen.
44. A polymer or a method as claimed in claim 42 or claim 43, wherein the antigen or immunogen is as defined in claim 31 or claim 32.
45. A polymer or a method as claimed in any one of claims 42 to 44, wherein the immune response comprises therapeutic and/or prophylactic vaccination.
46. A narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof for use with a substance that has pharmacological activity against a cancer for the treatment of the cancer and/or for inducing an immune response to the cancer.
47. A method of treating a cancer in a subject in need of such treatment, which comprises administering to the subject therapeutically effective amounts of a narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof and a substance that has pharmacological activity against the cancer.
48. A method of inducing an immune response to a cancer in a subject in need thereof, which comprises administering to the subject effective amounts of a narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof and a substance that has pharmacological activity against the cancer.
49. A polymer as claimed in claim 46 or claim 48, wherein the immune response comprises therapeutic and/or prophylactic vaccination.



- 91 -

50. A polymer or a method as claimed in any one of claims 34 to 49, wherein the polymer and the other substance are administered together or separately.

51. A polymer or a method as claimed in claim 50, wherein, when the polymer and the pharmacologically active substance are administered separately, they are administered substantially simultaneously or one is administered before the other.

52. A narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof for use as an immune potentiating adjuvant in the manufacture of a vaccine.

53. A narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof for use as an immune potentiating adjuvant in the manufacture of a vaccine that comprises an antigen or immunogen against which an immune response is to be induced.

54. In a method for the manufacture of a vaccine, the improvement comprising the use of a narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof as an immune potentiating adjuvant.

55. A complex, pharmaceutical preparation, method, or polymer as claimed in any one of the preceding claims, wherein the narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof has a polydispersity of 1.7 or less.

56. A complex, pharmaceutical preparation, method, or polymer as claimed in claim 55, wherein the polymer has a polydispersity of less than 1.4, for example, less than 1.2.

57. A complex, pharmaceutical preparation, method, or polymer as claimed in any one of the preceding claims, wherein the polymer has a molecular weight such that the polymer when present in the blood remains substantially in the circulating blood during and after passage through the kidney.

- 92 -

58. A complex, pharmaceutical preparation, method, or polymer as claimed in any one of the preceding claims, wherein the polymer has a molecular weight of 100,000 or less, for example, less than 100,00, for example, 80,000 or less, for example, 75,000 or less, for example, 65,000 or less, for example, 55,000 or less,  
5 for example, 45,000 or less, for example

59. A complex, pharmaceutical preparation, method, or polymer as claimed in any one of the preceding claims, wherein the polymer has a molecular weight of 4,000 or more, for example, 5,000 or more, for example, 10,000 or more, for  
10 example, 20,000 or more, for example, 30,000 or more, for example, 40,000 or more.

60. A complex, pharmaceutical preparation, method, or polymer as claimed in any one of the preceding claims, wherein the polymer has a molecular weight  
15 within the range of from 80,000 to 4,000, 75,000 to 5,000, 65,000 to 10,000, 55,000 to 10,000, 45,000 to 10,000, 50,000 to 4,000, 40,000 to 25,000 or 45,000 to 10,000.

61. A complex, pharmaceutical preparation, method, or polymer as claimed in  
20 any one of the preceding claims, wherein the polymer is produced by a process that involves hydrolysis of a polymer precursor.

62. A complex, pharmaceutical preparation, method, or polymer as claimed in claim 61, wherein the polymer including units derived from an acrylic acid or a salt  
25 thereof is produced by hydrolysis of a corresponding precursor polymer that has, in place of the hydrogen atom of the acrylate carboxylic acid in the units derived from an acrylic acid, a group that can be cleaved by hydrolysis to give the acid.

63. A complex, pharmaceutical preparation, method, or polymer as claimed in  
30 claim 62, wherein a group that can be cleaved by hydrolysis is, for example, an appropriate leaving group, for example, an electron withdrawing group, for example, an acylating group, which is preferably a carboxylate activating, generally selected from the group consisting of N-succinimidyl, pentachlorophenyl,

- 93 -

pentafluorophenyl, para-nitrophenyl, dinitrophenyl, N-phthalimido, N-bornyl, cyanomethyl, pyridyl, trichlorotriazine, 5-chloroquinolino, and imidazolyl groups, preferably an N-succinimidyl or imidazolyl group, and especially an N-succinimidyl group.

5

64. A complex, pharmaceutical preparation, method, or polymer as claimed in any one of claims 61 to 63, wherein hydrolysis is carried out using a basic agent, for example, an alkali metal or alkaline earth metal base, for example, a sodium, potassium, caesium, calcium, magnesium, or lithium base. Such a base may be, for example, a hydroxide, carbonate or hydrogen carbonate, for example, sodium hydroxide.

10

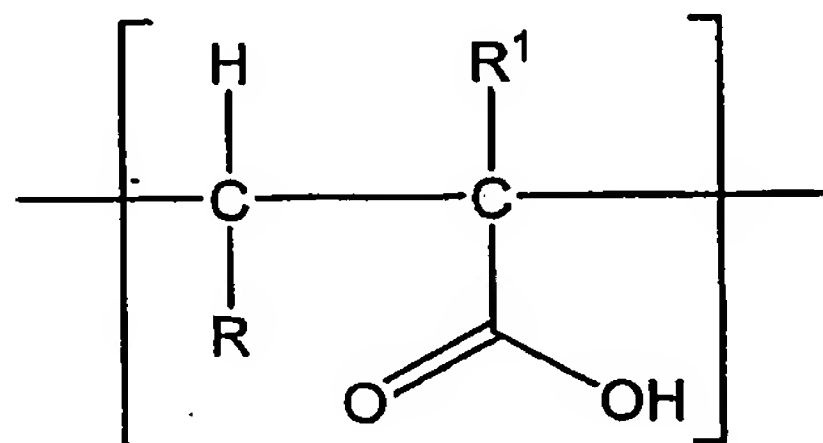
65. A complex, pharmaceutical preparation, method, or polymer as claimed in any one of the preceding claims, wherein the polymer is a poly(methacrylic acid) or a salt thereof.

15

66. A complex, pharmaceutical preparation, method, or polymer as claimed in claim 65, wherein the poly(*N*-methacryloxysuccinimide) (PMOSu) is produced by homogeneous polymerisation of methacryloxysuccinimide using a copper mediated atom transfer radical polymerisation method.

20

67. A complex, pharmaceutical preparation, method, or polymer as claimed in any one of claims 1 to 64, wherein the polymer is or comprises unit (I)

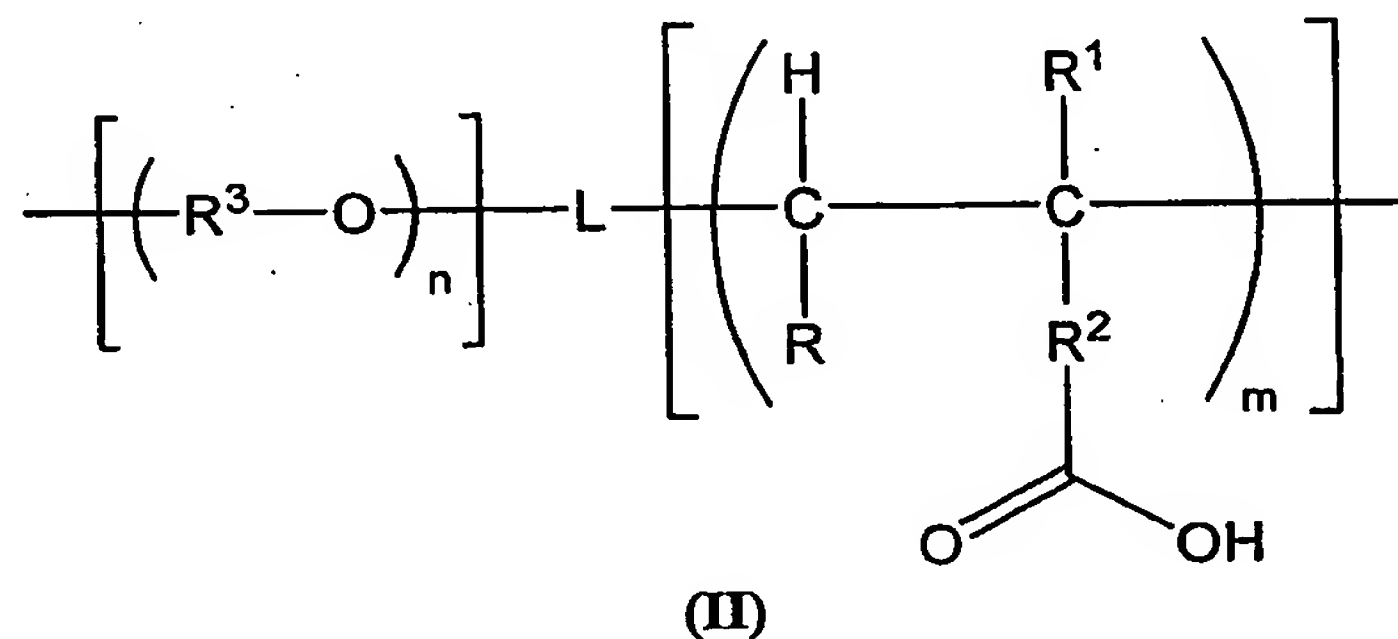


(I)

25

- 94 -

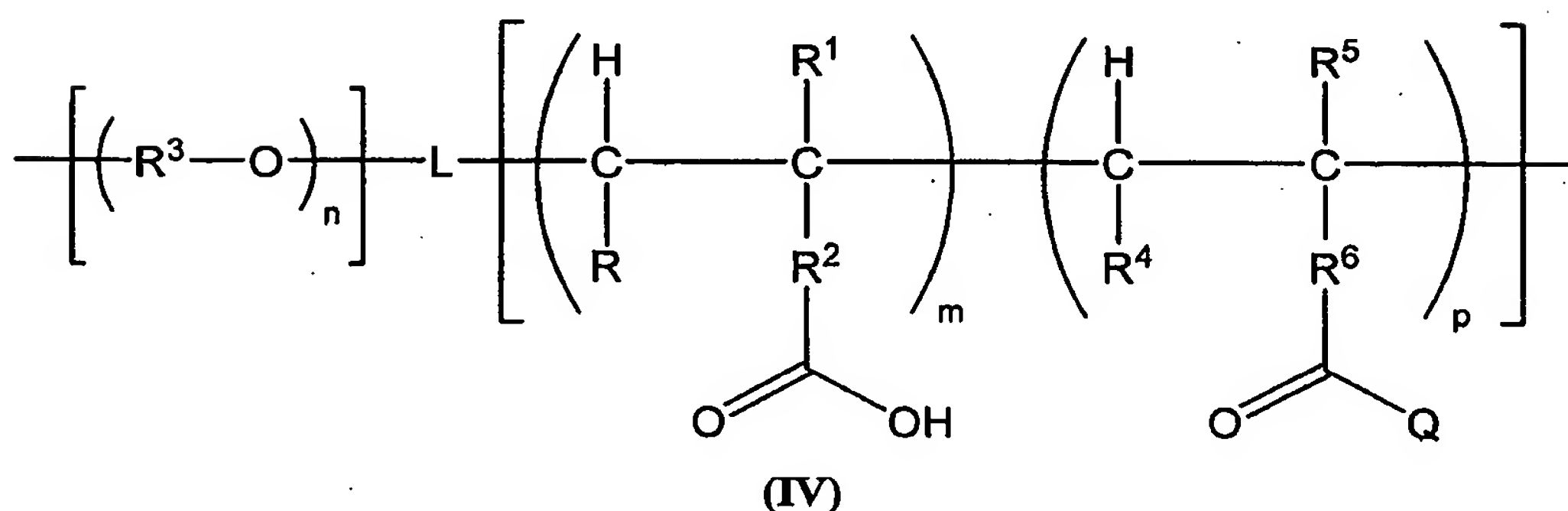
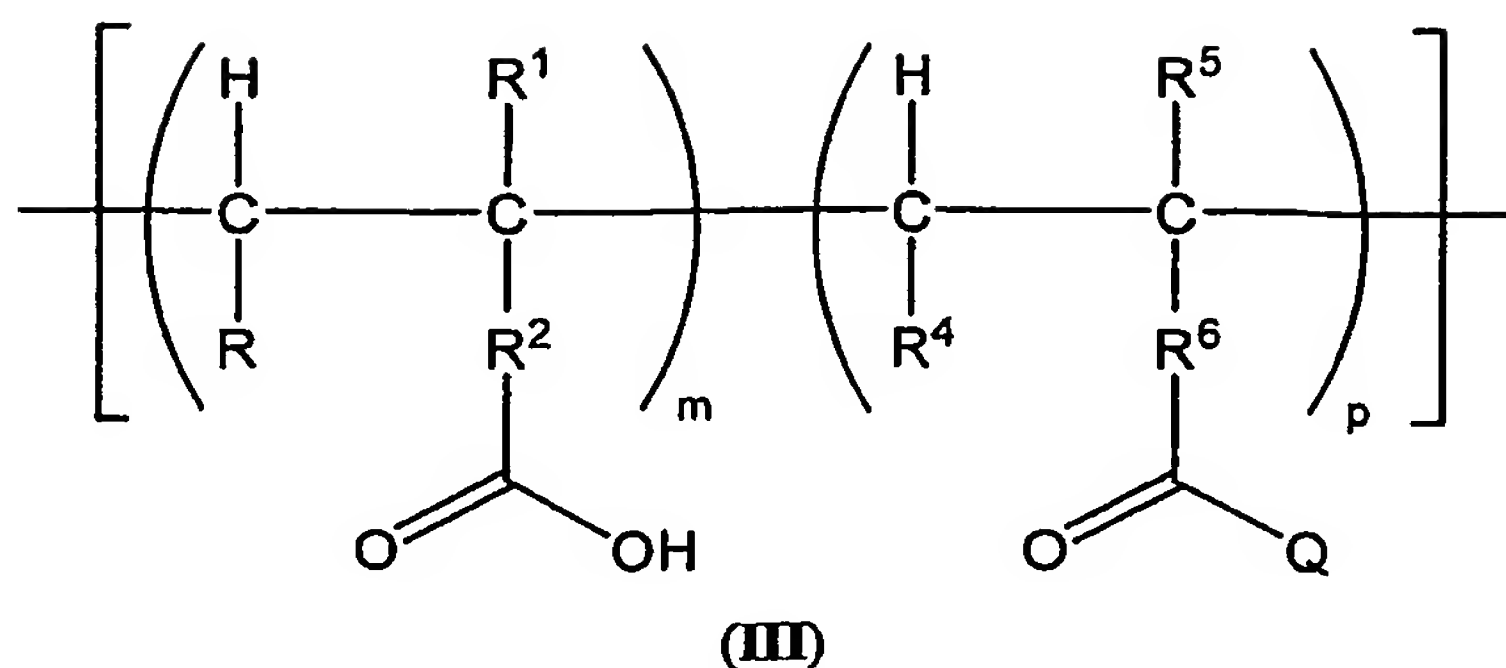
- wherein R is selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>18</sub>alkyl, C<sub>2</sub>-C<sub>18</sub> alkenyl, C<sub>7</sub>-C<sub>18</sub>aralkyl, C<sub>7</sub>-C<sub>18</sub>alkaryl, C<sub>6</sub>-C<sub>18</sub>aryl, carboxylic acid, C<sub>2</sub>-C<sub>18</sub>alkoxycarbony, C<sub>2</sub>-C<sub>18</sub>alkaminocarbonyl, or any one of C<sub>1</sub>-C<sub>18</sub>alkyl, C<sub>2</sub>-C<sub>18</sub> alkenyl, C<sub>7</sub>-C<sub>18</sub>aralkyl, C<sub>7</sub>-C<sub>18</sub>alkaryl, C<sub>6</sub>-C<sub>18</sub>aryl, carboxylic acid, C<sub>2</sub>-C<sub>18</sub>alkoxycarbony, C<sub>2</sub>-C<sub>18</sub>alkaminocarbonyl, substituted with a heteroatom within, or attached to, the carbon backbone; and R<sup>1</sup> is selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>6</sub>alkyl groups; and salts thereof, for example, alkali metal salts, for example, sodium salts, or ammonium salts thereof.
- 10 or the polymer is or comprises unit (II)



- in which R, R<sup>1</sup> and R<sup>2</sup> are defined as above; R<sup>3</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>18</sub>alkylene, C<sub>2</sub>-C<sub>18</sub>alkenylene, C<sub>7</sub>-C<sub>18</sub>aralkylene, C<sub>7</sub>-C<sub>18</sub>alkarylene, and C<sub>6</sub>-C<sub>18</sub>arylene; L is a divalent linker joining the blocks; and m and n is each an integer 1 or greater than 1.
- 15

68. A complex, pharmaceutical preparation, method, or polymer as claimed in any one of claims 1 to 64, wherein the polymer is or comprises unit (III) or (IV)
- 20

- 95 -



5

in which R, R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup>, L, m and n are defined as above, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are selected, independently, from the same groups as R, R<sup>1</sup> and R<sup>2</sup>, respectively; Q denotes a group that is not cleaved or is not substantially cleaved under the conditions used to produce the polymer; and p denotes an integer 1 or greater  
 10 than 1. If desired, Q may be a targeting group, i.e. a group that targets the polymer to a cell type, eg macrophages, or to an organ eg the liver.

69. A complex, pharmaceutical preparation, method, or polymer as claimed in any one of claims 1 to 68, wherein the polymer is produced by homogeneous  
 15 polymerisation of a succinimide precursor using an atom mediated atom transfer radical polymerisation method, for example, a copper mediated atom transfer radical polymerisation method:

70. A complex as defined in or referred to in any preceding claim, which  
 20 complex is produced by a method comprising hydrolysing polymer precursors to

- 96 -

form the polymer, wherein the hydrolysis is carried out in the presence of the component (i), (ii) or (iii) as defined in any one of the preceding claims .

71. A complex as claimed in claim 70, wherein the hydrolysis is carried out in is  
5 carried out using a basic agent, for example, an alkali metal or alkaline earth metal base, for example, a sodium, potassium, caesium, calcium, magnesium, or lithium base. Such a base may be, for example, a hydroxide, carbonate or hydrogen carbonate, for example, sodium hydroxide.

10 72. A complex as claimed in claim 1, which comprises a substance that has pharmacological activity against leishmaniasis and a narrow molecular weight distribution polymer that includes units derived from an acrylic acid or a salt thereof.

15 73. A complex as claimed in claim 72, wherein the pharmacologically active substance is amphotericin B.

74. A complex as claimed in claim 72 or claim 73, wherein the polymer is as  
20 defined in any one of claims 55 to 71.

75. A pharmaceutical preparation that comprises a complex as claimed in any one of claims 72 to 74 in admixture with a pharmaceutically suitable carrier and optionally a delivery system adjuvant.

25 76. A complex as claimed in any one of claims 72 to 74 or a pharmaceutical preparation as claimed in claim 75, for use in the treatment of leishmaniasis in any of its clinical forms.

30 77. A method of treating a leishmaniasis in a subject in need of such treatment, which comprises administering to the subject a therapeutically effective amount of a complex as claimed in any one of claims 72 to 74 or a pharmaceutical preparation as claimed in claim 75.